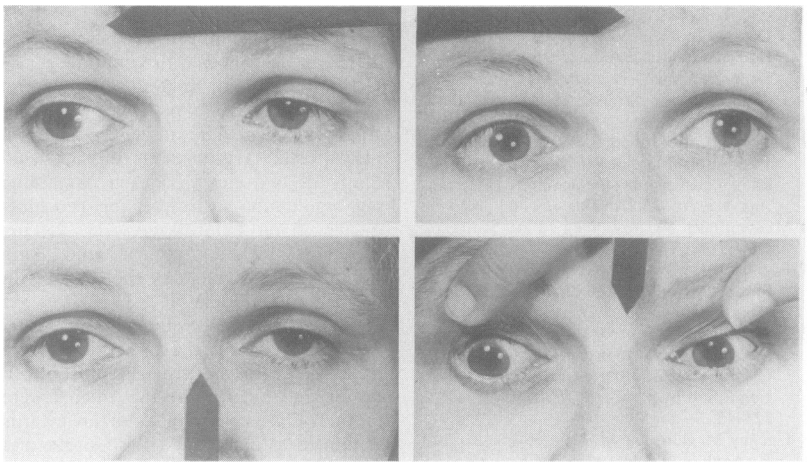

Fig 1 *Patient on day after admission attempting maximum gaze in the directions shown by arrows. Appearance in primary position of gaze identical to that on attempted upgaze (lower left).*

Walsh and O'Doherty[3] state that there should be (1) a history of typical migraine, (2) ophthalmoplegia involving one or more nerves on one side or alternating sides, and (3) exclusion of other causes by arteriography, surgery or necropsy.

The condition is uncommon, affecting approximately 1 in 600 migraine sufferers.[4] Patients are usually under 30 years of age, and have longstanding migraine. Following a headache, which is almost always periorbital, ptosis and oculomotor palsy develop. Pupillary paralysis is almost invariable.[4,5] Recovery occurs over days to months but recurrences may result in permanent deficit. Abducens nerve is involved alone in approximately 10% of cases,[6] and occasionally oculomotor palsy is accompanied by trochlear,[7] trigeminal,[8] facial,[9] or hypoglossal[10] nerve involvement.

Ocular paralysis usually seems to result from a peripheral lesion, but the pathophysiology has been debated. Possible mechanisms include direct pressure on ocular motor nerves[3] or occlusion of the small vessels supplying them[11] due to carotid artery oedema. Angiographic narrowing of the ipsilateral intracavernous carotid has been demonstrated in this disorder.[3]

Ophthalmoplegic migraine involving episodic paralysis of convergence[12] or convergence and upgaze[13] has rarely been reported. These instances suggest that ocular paralysis occasionally results from brainstem involvement.

The current case fulfils established criteria for diagnosis of ophthalmoplegic migraine. There was no definite evidence of other diseases which cause ophthalmoplegia and the minor CSF protein abnormalities were non-specific. In particular there were no other features suggesting multiple sclerosis or Miller-Fisher syndrome.

Of specific interest was the bilateral involvement. While there have been isolated reports[3] of ocular paralysis alternating sides in successive migraine attacks, bilateral involvement in a single episode has not, to our knowledge, been reported. Although no lesion was demonstrated, central pathology was considered unlikely as such a lesion would have to involve both midbrain and pons, and other clinical evidence of this was lacking. In addition, both levator palpebrae superioris muscles are believed to be innervated by a single midline nucleus and involvement of this would produce bilateral ptosis.[14] Finally, the recovery of eye movements proceeded asymmetrically. We thus suspect ophthalmoplegia resulted from bilateral peripheral lesions, possibly within the cavernous sinuses.

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Accepted 6 February 1989

Seizures as the initial manifestation of paralytic rabies

Sir: Typical phobic spasms in the form of aerophobia and hydrophobia are helpful signs in making a diagnosis in patients with encephalitic rabies. These signs, however, do not necessarily persist throughout the whole clinical course of the diseases. They may present in only half of the cases of paralytic rabies.[1] The clinical diagnosis of rabies can thus be extremely difficult. We here describe a patient with rabies who had paralysis resembling the Guillain Barré syndrome (GBS) and who initially presented with absence like seizures. She had no aerophobia

or hydrophobia. A postmortem study of rabies viral antigen distribution was performed by immunohistochemical techniques.

A 15 year old Thai female was well until 7 days previously, when she experienced abdominal pain associated with watery diarrhoea and vomiting. Abdominal symptoms soon disappeared and diarrhoea subsided after 48 hours. Her mother then began to notice that she developed occasional episodes of unresponsiveness and blank stare with eyes rolling upward during which she was unable to perform or to continue tasks for several seconds. The episodes subsided spontaneously and recurred many times during the day. She had no memory of these attacks. Within four days prior to admission, these symptoms recurred more frequently with more prolonged episodes. Persistent tremulousness of both hands and slurred speech were observed. She was alert and coherent during symptom free periods. There was no improvement after ingestion of food or sugar. Two days before entry, she was seen by a physician and received diazepam intramuscularly. Her symptoms of episodic blank spells improved for about one hour. One day before admission, she was noted to have inspiratory spasms accompanied by generalised piloerection and weakness of all limbs. On the day of admission, she was incontinent of urine. Walking was still possible with support. She was able to drink and eat without difficulty. When admitted to Chulalongkorn University Hospital she was fully conscious. Her temperature was 38·2°C, her blood pressure was 120/70 mm Hg, and the pulse rate was 110 beats per minute. Respirations were irregular and characterised by inspiratory spasms. No cyanosis, anaemia, or jaundice was observed. Mentation was normal, but was interrupted by brief episodes of blank spells lasting several seconds. The patient had bilateral facial weakness of lower motor neuron type with dysarthric speech. The gag reflex was present. Minimal dysphagia at attempts to drink water was noted. There was no aerophobia, hydrophobia or hypersalivation. Other cranial nerves were intact. Motor power examination revealed bilateral and symmetrical weakness of both upper and lower limbs. This was most marked at the proximal group with 3/5 MRC grading as compared with 4/5 of the distal group. Tremor of both hands was observed on postural maintenance. Pinprick and vibratory sensations were preserved. Deep tendon reflexes were all absent. Plantar responses were bilaterally flexor. An indwelling catheter was inserted.

The urine was normal. The haematocrit was 0·4 (40%); the white-cell count was 9·6 $\times$ 10^9/L (9·6 $\times$ 10^3/mm^3) with 69% neutrophils, 31% lymphocytes. Platelets were adequate and the erythrocyte sedimentation rate was 20mm per hour. Serum urea nitrogen, creatinine as well as liver function tests were normal. The sodium level was 131 mmol, the potassium 3·6 mmol, the chloride 92 mmol, and the carbon dioxide 15·5 mmol/l. The EEG showed a background activity of alpha range and periodic spike potentials at the temporal areas. Chest radiographs and an electrocardiogram were normal. A lumbar puncture showed clear liquid. The initial pressure was 90 mm H_2O, there were 5 lymphocytes. Glucose level was 4·2 mmol/l (76 mg/dl), and proteins were 1·4 g/l (140 mg/dl). Results of a Gram's stain and India ink preparation and cultures were negative. On hospital day 2, alternating intervals of confusion and drowsiness developed. During the confusional state, she appeared extremely agitated and disoriented. This happened without any warning, lasted only for minutes, and was accompanied by fixed and dilated pupils and generalised piloerection. Between these episodes of wild agitation, the patient became drowsy but was arousable. Upward tonic deviation of eyes occurred with increased frequency. Spontaneous inspiratory spasms, noted since the day of admission now occurred every few minutes and lasted about 5 seconds each. Bilateral facial weakness was complete and the gag reflex was totally absent. Marked hypersalivation was noted. Myoedema could be demonstrated by percussion at the chest, deltoid and thigh regions with a tendon hammer. She barely moved her legs and arms. Sensory function was still preserved. By the end of this day, spontaneous respiration was inadequate requiring ventilatory support. Further questioning of her parents revealed a history of a dog bite on her fingers 3 months previously. She received appropriate wound care but no rabies post-exposure prophylaxis. The anti-rabies antibody titre by rapid fluorescent focus inhibition test (RFFIT) of the serum was 1·4 IU/l. The spinal fluid revealed no detectable rabies antibody.

Irritability was gradually replaced by depression of consciousness on day 3. She opened her eyes for 10 seconds after being aroused. Breathing was totally dependent on the ventilator. Intermittent spasms of accessory respiratory muscles of the neck and of the diaphragm were still present. During the next 6 days, her condition deteriorated to the point where she was completely unresponsive with flaccid quadriplegia. High fever persisted in the range of 38 to 40·5°C and was partially relieved by the use of acetaminophen. Violent convulsive seizures appeared on hospital day 5 and were partly controlled by intravenous phenytoin and diazepam. Oculocephalic reflex and pupillary light reaction were intact. Intermittent contraction of sternocleidomastoids continued and percussion myoedema was still evident. On hospital day 6, sinus tachycardia followed by supraventricular tachycardia developed and severe hypotension supervened. She died on the 9th hospital day.

Rabies antigen distribution was studied by the avidin-biotin immunohistochemical technique[2] using equine rabies antibody (Becton Dickinson and Co., Cockeysville, MD). It was performed on formalin-fixed tissue from the brain, brainstem and cerebellum, spinal cord. Controls included nonimmune horse serum as a primary antibody and normal brain. These studies demonstrated the presence of rabies viral antigen in all examined areas. Diffuse distribution did not only occur in neurons, but also in cells consistent in appearance with astrocytes and oligodendrocytes. The degree of involvement of these glial cells was roughly similar to that of neurons. Inflammation was scant in relation to the amount of viral antigen, and was not limited to the spinal cord. Satellitosis, neuronal degeneration and glial nodules were rarely observed.

Paralytic rabies is difficult to diagnose because of its presentation which resembles GBS. This was tragically demonstrated in several corneal transplant cases.[3-5] The major cardinal signs of encephalitic rabies: aerophobia and hydrophobia, alternating intervals of full comprehension, agitation, confusion, and signs of autonomic dysfunction such as hypersalivation, usually appear late or not at all in paralytic rabies.[1,6] The most striking clinical difference between encephalitic and paralytic rabies is the relative sparing of consciousness in the latter group. Quadriparesis with predominant involvement of proximal muscles, fever, loss of deep tendon reflexes and urinary incontinence are universal findings in patients with paralytic rabies. Sensory functions are intact. However, presentation as an ascending myelitis with sensory loss to the thoracic level has been observed.[7] The helpful signs of paralytic rabies during the early phase are percussion myoedema and piloerection.[8] The presence of pure motor weakness, fluctuating consciousness and urinary incontinence help to differentiating paralytic rabies from sporadic as well as post-rabies vaccination induced GBS. Whe coma supervenes, both forms of rabies become indistinguishable. However, contraction of the sterno-

cleidomastoids may still continue intermittently in both forms if the patient is carefully observed.

Our patient had symptoms compatible with paralytic rabies. However, the initial presentation with seizures resulted in delay in diagnosis. Clinical seizures of cortical origin were extremely rare in our experience of more than 40 rabies patients (by Hemachudha and Manutsathit, unpublished data). Only one patient who received intensive respiratory support and had severe hyponatremia had a seizure during the preterminal phase. Opistothonos or convulsions during hydrophobic spasms have been described,[9] but not as an initial presentation. Attempts to make a diagnosis of human rabies in life by immunofluorescent testing for rabies virus antigen in corneal or salivary smears, or from nuchal skin or brain biopsy, and efforts to detect antibody to rabies virus in the serum or spinal fluid, were all disappointing during the early clinical stage of the disease.[6] Antibody to rabies virus by RFFIT was demonstrated in this case 9 days after the onset of disease. The presence of rabies antigen of comparable amount in both neurons and glial cells was surprising. Study of rabies virus distribution in six other patients (four encephalitic and two paralytic cases) showed neuron to be the almost exclusive target of infection (Manuscript submitted). Inclusion bodies in astrocytes have been regarded as an uncommon finding on light microscopy.[10 11] Only 17% of human rabies cases reported by Tangchai *et al*[10] were found to have inclusion body positive astrocytes. These were mostly in the floor of the third ventricle, paraventricular area and brainstem. It is not known whether seizure activity can be induced by the presence of virus in glial cells.

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Accepted 24 February 1989

Matters arising

Peripheral neuropathy complicating pancreatitis

We were interested in the observations of Gross *et al*.[1] In 1970, we reported a case of a 30 year old sportsman who presented with acute pancreatitis, which was treated by surgery. Immediately after the operation, the patient developed encephalopathy characterused by a confusional state. Within a few days, a severe sensorimotor polyneuritis had led to quadriplegia. Nerve biopsy demonstrated a very severe axonopathy (reported at the VI Congrés International de Neuropathologie, 1970). The neuropathy disappeared completely over the next few months, followed by complete remission of the encephalopathy.

Although all reported cases have had acute pancreatitis, there are some notable differences between our case and that reported by Gross *et al*. The neuropathy in our patient appeared within a few days of the onset of the pancreatitis, although in other cases, the first signs of neuropathy were only observed some weeks after the pancreatitis. Our patient was not diabetic, and was not taking metronidazole or receiving parenteral nutrition. This would tend to rule out an aetiology involving significant vitamin deficiency. These conditions of onset also rule out the so-called "critically ill polyneuropathy".[2] In addition, it is noteworthy that the acute pancreatitis in our patient was accompanied by involvement of both central (transient encephalopathy) and peripheral nervous systems. We feel that a peripheral neuropathy may, in some circumstances, result from an acute pancreatic lesion. However, further cases will need to be identified before a causal link can be established.

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The conduction velocities of peripheral nerve fibres conveying sensations of warming and cooling

Sir: Evidence that in man the sensations of warmth and cooling are conveyed by different fibres is indirect.[1] Fowler *et al*[1] using reaction times to supramaximal heat and cold stimuli in normal controls recently demonstrated that the two modalities were conducted at different velocities suggesting that cooling was subserved by small myelinated and warming by unmyelinated fibres. We provide objective evidence that dissociated loss of warming and cooling sensation exists in diseases as seen in three patients with peripheral neuropathy associated with the acquired immunodeficiency syndrome. Thermal thresholds[2] were tested using